

10/526978
DT01 Rec'd PCT/PTO 07 MAR 2005

AMENDMENT TO THE CLAIMS

LISTING OF CLAIMS:

Claims 1-74 (cancelled)

1. (Currently amended) An isolated nucleic acid encoding a mutant subtype 2 metabotropic glutamate receptor (~~mutant mGluR2~~) which comprises an amino acid sequence selected from the group consisting of SEQ.ID.NOS.:1-7, and SEQ.ID.NO.:8, wherein said.

2. (Currently amended) A composition comprising an isolated nucleic acid containing a sequence encoding a mutant subtype 2 metabotropic glutamate receptor as claimed in claim 1, wherein said isolated nucleic acid sequence is selected from the group consisting of:

- a) SEQ.ID.NOS.:9-16;
- b) a nucleic acid compound complementary to any sequence of (a); and
- c) a fragment of (a) or (b) that is at least 144 base pairs in length which will selectively hybridize to human genomic DNA encoding a human metabotropic glutamate receptor, and which will encode for the section of the mutant mGluR2 comprising altered amino acids at in at least one of positions 688, 689 and 735.

3. (Canceled)

4. (Canceled)

5. (Canceled)

6. (Canceled)

7. (Canceled)

8. (Currently amended) An expression vector ~~capable of producing a mutant mGluR2 receptor or a fragment thereof in a host cell which comprises a~~ comprising the nucleic acid of ~~as claimed in claim 2 in combination with regulatory elements necessary for expression of the nucleic acid in a suitable~~ the host cell.

9. (Currently amended) The expression vector of claim 8, wherein the host cell for use in a host cell wherein the host cell is of mammalian origin a mammalian cell line.

10. (canceled) The expression vector of claim 9 which comprises a CMV promoter.

11. (canceled) The expression vector of claim 10 which further comprises an adenovirus late promoter.

12. (canceled) The expression vector of claim 11 wherein the mammalian cell line is the HEK-293 cell line.

13. (canceled) A transfected host cell harboring an expression vector as claimed in claim 8.

14. (canceled) A transfected host cell as claimed in claim 13 which is a transfected mammalian cell line.

15. (canceled) A transfected host cell as claimed in claim 14 which is HEK-293 transfected with pCDNA3.1.

16. (Currently amended) An isolated mutant mGluR2 receptor which comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 1-8, SEQ.ID.NOS.:1-7, and SEQ.ID.NO:8 wherein said mutant mGluR2 is characterized as being capable of depotentiating glutamate receptor activity relative to wild-type mGluR2.

17. (Currently amended) A method for producing a mutant mGluR2 protein comprising the steps of:

a) expressing a nucleic acid molecule comprising a sequence of nucleotides that encode a recombinant mutant protein comprising an amino acid sequence ~~gene sequence~~ is selected from the group consisting of SEQ.ID.NOS.:9-16, and conservative variants thereof SEQ ID NOS: 1-8, in a suitable host cell under conditions favoring expression of said mutant protein ~~such that a recombinant protein comprising any of SEQ.ID.NO.:1-8 is expressed; and~~

b) purifying said recombinant protein by any suitable method.

18. (Canceled)

19. (Currently amended) A substantially pure mutant metabotropic glutamate receptor protein designated mGluR2 comprising an amino acid substitution at a selected position within an amino acid sequence sufficient to enable said mutant to depotentiate ~~A mutant form of GPCR class II receptor mGluR2 comprising a substitution of aspartic acid for asparagine at amino acid position 735 of said mGluR2 (SEQ.ID.NO.:1), whereby said mutant form depotentiates~~ glutamate receptor activity by altering an allosteric site associated with a transmembrane region 5 of said mGluR2 relative to wild-type mGluR2.

20. (Currently amended) The ~~A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution comprises~~ comprising a substitution of leucine for serine at amino acid position 688 as set forth in SEQ ID NO:4 of said mGluR2 (SEQ.ID.NO.:4), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane region 4 of said mGluR2.

21. (Currently amended) The ~~A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution comprises~~ comprising a substitution of valine for glycine at amino acid position 689 as set forth in SEQ ID NO:3 of said mGluR2 (SEQ.ID.NO.:3), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane region 4 of said mGluR2.

22. (Currently amended) The ~~A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution comprises~~ comprising a substitution of leucine for serine at amino acid position 688 and aspartic acid for asparagine at amino acid position 735 of SEQ ID NO:6 of said mGluR2 (SEQ.ID.NO.:6), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR2.

23. (Currently amended) The ~~A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution~~

~~comprises~~ comprising a substitution of valine for glycine at amino acid position 689 ~~of said mGluR2~~ and aspartic acid for asparagine at amino acid position 735 of SEQ ID NO:2 of said mGluR2 (SEQ.ID.NO.:2), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR2.

24. (Currently amended) The A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution comprises ~~comprising~~ a substitution of leucine for serine at amino acid position 688 ~~of said mGluR2~~, valine for glycine at amino acid position 689 of said mGluR2, and aspartic acid for asparagine at amino acid position 735 of SEQ ID NO:3 of said mGluR2 (SEQ.ID.NO.3), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR2.

25. (Currently amended) The A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution comprises ~~comprising~~ a substitution of leucine for serine at amino acid position 688 ~~of said mGluR2~~ and valine for glycine at amino acid position 735 of SEQ ID NO:5 of said mGluR2 (SEQ.ID.NO.:5), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane region 4 of said mGluR2.

26. (Currently amended) The A mutant form of GPCR class II receptor mGluR2 of claim 19, wherein said amino acid substitution comprises ~~comprising~~ a substitution of leucine for serine at amino acid position 688 ~~of said mGluR2~~, valine for glycine at amino acid position 689 of said mGluR2, threonine for alanine at amino acid position 733 of said mGluR2, and aspartic acid for asparagine at amino acid position 735, of SEQ ID NO:8 of said mGluR2 (SEQ.ID.NO.:8), whereby said mutant form and said mutant protein depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR2.

27. (Currently amended) The A~~n~~ isolated nucleic acid molecule of claim 1, comprising a sequence of nucleotides ~~encoding a mutant form of mGluR2, said~~

~~isolated nucleic acid molecule~~ selected from the group consisting of SEQ.ID.NOS.:9-16;
~~wherein said mutant form of mGluR2 depotentiates glutamate activity.~~

28. (Original) The isolated nucleic acid molecule of claim 27 further comprising a nucleotide sequence encoding a polypeptide fused to an amino or carboxy terminal of said isolated nucleic acid molecule.

29. (Canceled)

30. (Canceled)

31. (Canceled)

32. (Currently amended) The A mutant form of GPCR class II
~~receptor mGluR2 of claim 19, wherein said amino acid substitution comprises~~ comprising a
substitution of aspartic acid for asparagine at amino acid position 744 of SEQ ID NO:33 ~~of~~
~~said mGluR2 (SEQ.ID.NO.:33), whereby said mutant form and said mutant protein~~
depotentiates glutamate receptor activity by altering an allosteric site associated with
transmembrane region and 5 of said mGluR3.

33. (Currently amended) A substantially pure mutant
metabotropic glutamate receptor protein designated mGluR2 comprising an amino
acid substitution at a selected position within an amino acid sequence sufficient to
enable said mutant to depotentiate ~~A mutant form of GPCR class II receptor~~
~~mGluR3 comprising a substitution of leucine for serine at amino acid position 697~~
~~of said mGluR3 (SEQ.ID.NO.:36), whereby said mutant form depotentiates~~
glutamate receptor activity by altering an allosteric site associated with a
transmembrane region 5 of said mGluR3 relative to wild-type mGluR3.

34. (Currently amended) The A mutant form of GPCR
~~class II receptor mGluR3 of claim 33 herein said amino acid substitution comprises~~
~~comprising~~ a substitution of valine for glycine at amino acid position 698 as set
forth in SEQ ID NO:39 ~~of said mGluR3 (SEQ.ID.NO.39), whereby said mutant~~
~~form and said mutant protein~~ depotentiates glutamate receptor activity by altering
an allosteric site associated with transmembrane region 4 of said mGluR3.

35. (Currently amended) The A mutant form of GPCR
~~class II receptor mGluR3 of claim 33, wherein said amino acid substitution~~

~~comprises~~ ~~comprising~~ a substitution of leucine for serine at amino acid position 688 of said mGluR3 and aspartic acid for asparagine at amino acid position 735 of SEQ ID NO: 38 of said mGluR3 (SEQ.ID.NO.:38), ~~whereby said mutant form and said mutant protein~~ depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR3.

36. (Currently amended) ~~The A mutant form of GPCR class-II receptor~~ mGluR3 of claim 33, wherein said amino acid substitution ~~comprises~~ ~~comprising~~ a substitution of valine for glycine at amino acid position 689 of said mGluR3 and aspartic acid for asparagine at amino acid position 735 of SEQ ID NO: 34 of said mGluR3 (SEQ.ID.NO.:34), ~~whereby said mutant form and said mutant protein~~ depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR3.

37. (Currently amended) ~~The A mutant form of GPCR class-II receptor~~ mGluR3 of claim 33, wherein said amino acid substitution ~~comprises~~ ~~comprising~~ a substitution of leucine for serine at amino acid position 688 of said mGluR3, a substitution of valine for glycine at amino acid position 689 of said mGluR3, and a substitution of aspartic acid for asparagine at amino acid position 735 of SEQ ID NO: 35 of said mGluR3 (SEQ.ID.NO.:35), ~~whereby said mutant form and said mutant protein~~ depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane regions 4 and 5 of said mGluR3.

38. (Currently amended) ~~The A mutant form of GPCR class-II receptor~~ mGluR3 of claim 33, wherein said amino acid substitution ~~comprises~~ ~~comprising~~ a substitution of leucine for serine at amino acid position 688 of said mGluR3, and a substitution of valine for glycine at amino acid position 689 of said mGluR3 as set forth in SEQ ID NO: 37 of said mGluR3 (SEQ.ID.NO.:37), ~~whereby said mutant form and said mutant protein~~ depotentiates glutamate receptor activity by altering an allosteric site associated with transmembrane region 4 of said mGluR3.

39. (Currently amended) ~~The A mutant form of GPCR class-II receptor~~ mGluR3 of claim 33, wherein said amino acid substitution ~~comprises~~ ~~comprising~~ a substitution of leucine for serine at amino acid position 688 of said mGluR3, a substitution of valine for glycine at amino acid position 689

~~of said mGluR3~~, a substitution of threonine for alanine at amino acid position 733
~~of said mGluR3~~, and a substitution of aspartic acid for asparagine at amino acid
position 735 as set forth in SEQ ID NO: 40 of said mGluR3 (SEQ.ID.NO.:40),
~~whereby said mutant form and said mutant protein~~ depotentiates glutamate receptor
activity by altering an allosteric site associated with transmembrane regions 4 and 5
of said mGluR3

40. (Canceled)

41. (Canceled)

42. (Canceled)

43. (New) The A mutant form of GPCR class II receptor
mGluR2 of claim 19, wherein said amino acid substitution comprises ~~comprising~~ a
substitution of aspartic acid for asparagine at amino acid position 735 as set forth in
SEQ ID NO:1 of said mGluR2 (SEQ.ID.NO.:1), ~~whereby said mutant form and~~
said mutant protein depotentiates glutamate receptor activity by altering an
allosteric site associated with transmembrane region 5 of said mGluR2.

44. (New) The A mutant form of GPCR class II receptor
mGluR3 of claim 33 herein said amino acid substitution comprises ~~comprising~~ a
substitution of leucine for serine at amino acid position 697 as set forth in SEQ ID
NO:36 of said mGluR3 (SEQ.ID.NO.36), ~~whereby said mutant form and said~~
mutant protein depotentiates glutamate receptor activity by altering an allosteric
site associated with transmembrane region 5 of said mGluR3.